JC20 Rec'd PCT/PTO 09 MAY 2005

CLAIMS:

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- 1. A process for Identifying a compound which selectively induces the mitochondrial permeability transition (MPT) in proliferating cells, wherein said process comprises contacting a cell or cell extract with a compound, determining whether the compound binds to adenine nucleotide translocator (ANT), and determining whether the compound selectively induces the MPT in proliferating cells.
- 2. A process for screening a plurality of compounds to identify a compound which selectively induces MPT in proliferating cells, wherein said process comprises contacting a cell or a cell extract with the plurality of compounds, determining whether any of the compounds bind to ANT, and if so, separately determining for each of the plurality of compounds whether the compound selectively induces the MPT in proliferating cells.
- 3. The process of claim 1 or 2, wherein selectivity for proliferating cells is determined by comparing the effect of compounds identified as binding to ANT on the MPT in proliferating cells with the effect on the MPT in non-proliferating or growth quiescent cells.
- 4. The process of claim 1 or 2, wherein said determination of induction of the MPT involves measuring changes in Cytochrome C release.
- 5. The process of claim 1 or 2, wherein said determination of induction of the MPT involves measuring changes in cellular superoxide concentration.
- 6. A process of inducing MPT in a vertebrate, wherein the method comprises administering to the vertebrate a therapeutically effective amount of at least one compound identified in accordance with the process of any one of claims 1 to 5, or a therapeutically effective amount of a pharmaceutical composition comprising at least one of said compounds together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.
- 7. A process of inducing apoptosis in proliferating mammalian cells, comprising administering to the mammal an apoptosis-inducing amount of a compound identified in accordance with the process of any one of claims 1 to 5, or a therapeutically effective amount of a pharmaceutical composition comprising at least one of the compounds together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.
- 8. A process of inhibiting anglogenesis in a mammal, comprising administering to the mammal an anglogenesis-inhibiting amount of a compound identified in accordance with the process of any one of claim 1 to 5, or a therapeutically effective amount of a pharmaceutical composition comprising at least one of said compounds together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

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- 9. The process of any one of claims 1 to 8, wherein the compound is a dithiol reactive compound.
- 10. The process of any one of claims 1 to 8, wherein the compound has an arsenoxide (or arsenoxide equivalent) moiety.
 - 11. The process of claim 10, wherein the compound is of the formula (I):

$$A-[(XBX')_nB'-Y]_p \qquad (I)$$

wherein

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A comprises at least one pendant group;

 $(XBX')_nB'$ comprises a suitable linker group, wherein X is selected from the group consisting of -NR, -S(O)-, -S(O)2-, -S(O)2-, -S(O)2-, -C(O)-, -C(O)0-, -C(O

B is selected from the group consisting of C_1 - C_{10} alkylene, C_2 - C_{10} alkenylene, C_3 - C_{10} cycloalkylene, C_5 - C_{10} cycloalkenylene, C_3 - C_{10} heterocycloalkylene, C_5 - C_{10} heterocycloalkenylene, C_6 - C_{12} arylene, heteroarylene and C_2 - C_{10} acyl;

 $X' \text{ is selected from the group consisting of -NR-, -O-, -S-, -Se-, -S-S-, S(O)-, -OS(O)-, } \\ OS(O)O-, -OS(O)_2, -OS(O)_2O-, -S(O)O-, -S(O)_2-, -S(O)_2O-, -OP(O)(R_1)-, -OP(O)(R_1)O-, -OP(O)(R_1)O-, -C(O)-, -C(O)O-, -C(S)O-, -C(S)S-, -P(O)(R_1)-, -P(O)(R_1)O-, and } \\ OP(O)(R_1)OP(O)(R_1)O-, -C(O)-, -C(O)-, -C(O)O-, -C(S)O-, -C(S)S-, -P(O)(R_1)-, -P(O)(R_1)O-, and } \\ OP(O)(R_1)OP(O)(R_1)O-, -C(O)-, -C(O)-, -C(O)O-, -$

or is absent; wherein E is O, S, Se, NR or N(R)2+;

B' is selected from the group consisting of C_1 - C_{10} alkylene, C_2 - C_{10} alkenylene, C_3 - C_{10} cycloalkylene, C_5 - C_{10} cycloalkenylene, C_5 - C_{10} heterocycloalkylene, C_5 - C_{10} heterocycloalkenylene, C_6 - C_{12} arylene, and heteroarylene or is absent; and wherein

each R is independently selected from the group consisting of hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkenyl, C_3 - C_{10} alkenyl, C_3 - C_{10} heterocycloalkenyl, C_6 - C_{12} aryl, heteroaryl, C_8 - C_{10} and C_2 - C_{10} acyl;

R' is the same as R or two R' may be taken together with the nitrogen atoms to which they are attached to form a 5 or 6-membered saturated or unsaturated heterocyclic ring;

each R₁ is independently selected from the group consisting of hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₅-C₁₀ cycloalkenyl, C₃-C₁₀ heterocycloalkenyl, C₆-C₁₂ aryl, heteroaryl, halo, OR₂ and N(R)₂;

each R₂ is independently selected from the group consisting of hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₅-C₁₀ cycloalkenyl, C₃-C₁₀ heterocycloalkenyl, C₆-C₁₂ aryl, heteroaryl and -C(O)R₅;

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each R_5 is independently selected from the group consisting of hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_3 - C_{10} heterocycloalkenyl, C_6 - C_{12} aryl, heteroaryl, C_1 - C_{10} alkoxy, C_3 - C_{10} alkenyloxy, C_3 - C_{10} alkenyloxy, C_5 - C_{10} cycloalkenyloxy, C_3 - C_{10} heterocycloalkyloxy, C_5 - C_{10} heterocycloalkenyloxy, C_6 - C_{12} aryloxy, heteroaryloxy, C_1 - C_{10} alkylthio, C_3 - C_{10} alkenylthio, C_3 - C_{10} alkenylthio, C_3 - C_{10} heterocycloalkylthio, C_5 - C_{10} cycloalkenylthio, C_5 - C_{10} heterocycloalkylthio, C_5 - C_{10}

wherein for each instance that B and/or B' is arylene, the substituents directly attached to the respective arylene rings (including arsenoxide or arsenoxide equivalent) may be in a para-, meta- or ortho- relationship; and

wherein each alkylene, alkenylene, alkynylene, cycloalkylene, cycloalkenylene, heterocycloalkylene, heterocycloalkenylene, arylene, heteroarylene and acyl may be independently substituted with hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_3 - C_{10} heterocycloalkyl, C_5 - C_{10} heterocycloalkenyl, C_6 - C_{12} aryl, heteroaryl, cyano, cyanate, isocyanate, OR_{2a} , SR_6 , nitro, arsenoxide, -S(O)R₃, -OS(O)R₃, -S(O)2R₃, -OS(O)2R₃, -P(O)R₄R₄, -OP(O)R₄R₄, -N(Rⁿ)₂, -NRC(O)(CH₂)_mQ, -C(O)R₅;

wherein R, R₁ and R₅ are as defined above; and

 R_{2a} is selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, $-S(O)R_3$, $-S(O)_2R_3$, $-P(O)(R_4)_2$, $N(R)_2$ and $-C(O)R_5$;

each R_3 is independently selected from the group consisting of hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_3 - C_{10} heterocycloalkyl, C_5 - C_{10} heterocycloalkenyl, C_6 - C_{12} aryl, heteroaryl, C_1 - C_{10} alkoxy, C_3 - C_{10} alkenyloxy, C_3 - C_{10} cycloalkyloxy, C_5 - C_{10} cycloalkenyloxy, C_3 - C_{10} heterocycloalkyloxy, C_5 - C_{10} heterocycloalkenyloxy, C_6 - C_{12} aryloxy, heteroaryloxy, C_1 - C_{10} alkylthio, C_3 - C_{10} alkenylthio, C_3 - C_{10} alkynylthio, C_3 - C_{10} cycloalkylthio, C_5 - C_{10} heterocycloalkenylthio, C_5 - C_{10} heterocycloalkenylthio, C_6 - C_{12} arylthio, heteroarylthio and C_7

each R₄ is independently selected from the group consisting of hydrogen, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_3 - C_{10} heterocycloalkenyl, C_6 - C_{12} aryl, heteroaryl, C_1 - C_{10} alkoxy, C_3 - C_{10} alkenyloxy, C_3 - C_{10} cycloalkyloxy, C_5 - C_{10} cycloalkyloxy, C_5 - C_{10} heterocycloalkyloxy, C_5 - C_{10}

heterocycloalkenyloxy, C_6 - C_{12} aryloxy, heteroaryloxy, C_1 - C_{10} alkylthio, C_3 - C_{10} alkenylthio, C_3 - C_{10} alkynylthio, C_3 - C_{10} cycloalkylthio, C_5 - C_{10} heterocycloalkylthio, C_5 - C_{10} heterocycloalkenylthio, C_6 - C_{12} arylthio, heteroarylthio, halo and $N(R)_2$;

 R_6 is selected from the group consisting of C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_5 - C_{10} heterocycloalkyl, C_5 - C_{10} heterocycloalkenyl, C_6 - C_{12} aryl, heteroaryl, C_1 - C_{10} alkylthio, C_3 - C_{10} alkenylthio, C_3 - C_{10} alkynylthio, C_3 - C_{10} cycloalkenylthio, C_5 - C_{10} cycloalkenylthio, C_3 - C_{10} heterocycloalkylthio, C_5 - C_{10} heterocycloalkenylthio, C_6 - C_{12} arylthio, heteroarylthio, -S(O)R₃, -S(O)₂R₃ and -C(O)R₅.

R" is the same as R or two R" taken together with the N atom to which they are attached may form a saturated, unsaturated or aromatic heterocyclic ring system;

Q is selected from halogen and -OS(O)₂Q₁; wherein Q₁ is selected from C₁-C₄ alkyl, C₁-C₄ perfluoroalkyl, phenyl, p-methylphenyl; and

m is 1 to 5,

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n is an integer from 0 to 20

Y comprises at least one arsenoxide or arsenoxide equivalent;

p is an integer from 1 to 10, and wherein the compound of formula (I) has more than 6 carbon atoms.

- 12. The process of claim 11, wherein A is selected from the group consisting of natural, unnatural and synthetic amino acids, hydrophilic amines, peptides, polypeptides, sugar residues, oligosaccharides, and thiol containing proteins, small acid residues, hydroxyl containing residues, or a combination thereof.
- 13. The process of claim 12, wherein said hydrophilic amine is selected from primary alkylamines, primary arylamines, primary aralkylamines, secondary alkylamines, secondary arylamines, tertiary alkylamines, tertiary arylamines and tertiary aralkylamines, and heterocyclic amines.
- 14. The process of claim 12 or 13, wherein A is selected from the group consisting of dipeptides, tripeptides, tetrapeptides, pentapeptides, glutathione, glucosamine, saccharides, disaccharides, oligosaccharides, wherein the sulfur atom of each sulfur containing residue may be optionally oxidised to form a sulfoxide or sulfone.
- 15. The process of claim 14, wherein A is selected from a peptide comprising one or more of cysteinylglycine, cysteic acid, aspartic acid, glutamic acid, lysine, and arginine; glucose, fructose, mannose, xylose, lyxose, galactose, hexose, sucrose, sorbose, galactosyl-sucrose, sorbitol, mannitol, and xylitol,
 - 16. The process of any one of claims 11 to 15, wherein

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X is selected from the group consisting of -C(O)-, -C(S)-, -C(O)O-, C(S)O-, and -C(S)S-, or is absent;

B is selected from the group consisting of C₁-C₅ alkylene, C₂-C₅ alkenylene, C₂-C₅ alkynylene, C₃-C₁₀ cycloalkylene, C₅-C₁₀ cycloalkenylene, C₆-C₁₂ arylene and C₂-C₅ acyl;

X' is selected from the group consisting of -O-, -S-, -NR-, -S-S-, -S(O)-, -S(O)₂-, $-P(O)(R_1)$ -, $-OP(O)(R_1)O$ -, -C(O)-, -C(O

n is 0, 1 or 2; and

B' is C_1 - C_5 selected from the group consisting of alkylene, C_2 - C_5 alkenylene, C_3 - C_{10} cycloalkylene, C_5 - C_{10} cycloalkenylene, and C_6 - C_{12} arylene, or is absent; and wherein

each R is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl, C₃-C₁₀ cycloalkyl, C₅-C₁₀ cycloalkenyl, C₆-C₁₂ aryl, OR₂ and C₂-C₁₀ acyl;

R' is the same as R;

each R_1 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, halo, OR_2 and $N(R)_2$;

each R_2 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, and -C(O) R_5 ;

each R_5 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, C_3 - C_5 alkynyloxy, C_3 - C_1 0 cycloalkyloxy, C_5 - C_1 0 cycloalkenyloxy, C_6 - C_{12} aryloxy, C_1 - C_5 alkylthio, C_3 - C_5 alkenylthio, C_3 - C_5 alkynylthio, C_3 - C_1 0 cycloalkylthio, C_5 - C_1 0 cycloalkenylthio, C_6 - C_1 2 arylthio, C_1 - C_1 3 and C_1 4 and C_1 5 alkylylthio, C_2 - C_1 6 cycloalkylthio, C_3 - C_1 7 cycloalkenylthio, C_5 - C_1 9 cy

wherein for each instance that B and/or B' is arylene, the substituents directly attached to the respective arylene rings (including arsenoxide or arsenoxide equivalent), may be in a para-, meta- or ortho- relationship, and

wherein each alkylene, alkenylene, alkynylene, cycloalkylene, cycloalkenylene, arylene, and acyl may be independently substituted with hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, cyano, halo, cyanate, isocyanate, OR_{2a} , SR_5 , nitro, arsenoxide, $-S(O)R_3$, $-OS(O)R_3$, $-S(O)_2R_3$, $-OS(O)_2R_3$, $-P(O)R_4R_4$, $-OP(O)R_4R_4$, $-N(R^n)_2$, $NRC(O)(CH_2)_mQ$, $-C(O)R_5$,

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$$R_4$$
 R $O^ I_+$ $P^ R_4$, $P^ R_4$, $P^ R_4$, $P^ R_4$ R_5 R_7 R_8

wherein R, R₁ and R₅ are as defined above; and

 R_{2a} is selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, -S(O)R₃, -S(O)₂R₃, -P(O)(R₄)₂, N(R)₂ and -C(O)R₅;

each R_3 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, C_3 - C_5 alkynyloxy, C_3 - C_1 0 cycloalkyloxy, C_5 - C_1 0 cycloalkenyloxy, C_6 - C_1 2 aryloxy, C_1 - C_5 alkynylthio, C_3 - C_5 alkenylthio, C_3 - C_5 alkynylthio, C_3 - C_1 0 cycloalkylthio, C_5 - C_1 0 cycloalkenylthio, C_6 - C_1 2 arylthio and C_1 0 and C_1 1.

each R_4 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, C_3 - C_5 alkenyloxy, C_3 - C_5 alkynyloxy, C_3 - C_{10} cycloalkyloxy, C_5 - C_{10} cycloalkenyloxy, C_6 - C_{12} aryloxy, C_1 - C_5 alkylthio, C_3 - C_5 alkenylthio, C_3 - C_5 alkynylthio, C_3 - C_5 cycloalkylthio, C_5 - C_5 cycloalkenylthio, C_6 - C_{12} arylthio, halo and $N(R)_2$;

 R_6 is independently selected from the group consisting of C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, C_1 - C_5 alkylthio, C_3 - C_5 alkenylthio, C_3 - C_5 alkynylthio, C_3 - C_{10} cycloalkylthio, C_5 - C_{10} cycloalkenylthio, C_6 - C_{12} arylthio, C_6 - C_{12} - C_6 - C_{12} - C_6 -C

R" is the same as R;

Q is selected from the group consisting of halogen and -OS(O)₂Q₁; wherein Q₁ is selected from C₁-C₄ alkyl, C₁-C₄ perfluoroalkyl, phenyl, p-methylphenyl;

m is 1 to 5.

17. The process of any one of claims 11 to 16, wherein

X is absent;

B is selected from the group consisting of C₁-C₅ alkylene, C₆-C₁₂ arylene and C₂-C₅ acyl;

X' is selected from the group consisting of -O-, -S-, -NR-, -S-S-, -S(O)-, -S(O)₂-, $-P(O)(R_1)$ -, -C(O)-, -C(O)O-, -C(S)O-, -S-, and

n is 0, 1 or 2; and

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B' is C₁-C₅ alkylene, C₆-C₁₂ arylene or is absent; and wherein

each R is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₂ aryl, OR₂ and C₂-C₅ acyl;

R' is the same as R;

each R₁ is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₂ aryl, halo, OR₂ and N(R)₂;

each R₂ is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₂ aryl and -C(O)R₅;

each R_5 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, C_3 - C_5 alkenyloxy, C_3 - C_{10} cycloalkyloxy, C_5 - C_{10} cycloalkenyloxy, C_6 - C_{12} aryloxy, C_1 - C_5 alkylthio, C_3 - C_5 alkenylthio, C_3 - C_{10} cycloalkenylthio, C_6 - C_{12} arylthio, C_6 - C_{12} arylthio, C_7 - C_7 -

wherein for each instance that B and/or B' is arylene, the substituents directly attached to the respective arylene rings (including arsenoxide or arsenoxide equivalent) may be in a para-, meta- or ortho- relationship, and

wherein each alkylene, alkenylene, alkynylene, cycloalkylene, cycloalkenylene, arylene, and acyl may be independently substituted with hydrogen, C₁-C₅ alkyl, C₂-C₅ alkenyl, C₂-C₅ alkynyl,

 C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, halo, cyano, cyanate, isocyanate, OR_{2a} , SR_6 , nitro, arsenoxide, $-S(O)R_3$, $-OS(O)R_3$, $-OS(O)_2R_3$, $-OS(O)_2R_3$, $-P(O)R_4R_4$, $-OP(O)R_4R_4$, $-N(R'')_2$, $-NRC(O)(CH_2)_mQ$, $-C(O)R_5$,

wherein R, R₁ and R₅ are as defined above; and

 R_{2a} is selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_3 - C_{10} cycloalkyl, C_6 - C_{12} aryl, $-S(O)R_3$, $-S(O)_2R_3$, $-P(O)(R_4)_2$ and $-C(O)R_5$;

each R_3 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_3 - C_{10} cycloalkyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, C_3 - C_{10} cycloalkyloxy, C_6 - C_{12} aryloxy, C_1 - C_5 alkylthio, C_3 - C_{10} cycloalkylthio, C_6 - C_{12} arylthio and $N(R)_2$;

each R_4 is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_3 - C_{10} cycloalkyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, C_3 - C_{10} cycloalkyloxy, C_6 - C_{12} aryloxy, halo and $N(R)_2$;

 R_6 is selected from the group consisting of C_1 - C_5 alkyl, C_3 - C_{10} cycloalkyl, C_6 - C_{12} aryl, C_1 - C_5 alkylthio, C_3 - C_{10} cycloalkylthio, C_6 - C_{12} arylthio, C_6 - C_{12} - C_6 - C_7 -

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R" is the same as R;

Q is selected from halogen and -OS(O)₂Q₁; wherein Q₁ is selected from C₁-C₄ alkyl, C₁-C₄ perfluoroalkyl, phenyl, p-methylphenyl; and

m is 1 to 5.

18. The process of any one of claims 11 to 17, wherein

X is absent:

B is selected from the group consisting of C_1 - C_5 alkylene, C_6 - C_{12} arylene and C_2 - C_5 acyl; X' is selected from the group consisting of -O-, -S-, -NR-, -C(O)-, and -C(O)O-, or is absent; n is 1; and

B' is C₁-C₅ alkylene, C₆-C₁₂ arylene or is absent; and

R is selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₆-C₁₂ aryl and C₂-C₅ acyl; wherein for each instance that B and/or B' is arylene, the substituents directly attached to the respective arylene rings (including arsenoxide or arsenoxide equivalent), may be in a parameta- or ortho- relationship, and

wherein each alkylene, arylene, and acyl may be independently substituted with hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_{10} cycloalkyl, C_5 - C_{10} cycloalkenyl, C_6 - C_{12} aryl, halo, cyano, cyanate, isocyanate, OR_{2a} , SR_6 , nitro, arsenoxide, $-S(O)R_3$, $-S(O)_2R_3$, $-P(O)R_4R_4$, $-N(R^*)_2$, $-NRC(O)(CH_2)_mQ$, $-C(O)R_5$,

wherein each R is independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_6 - C_{12} aryl and C_2 - C_5 acyl;

 R_{2a} is selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_6 - C_{12} aryl, -S(O)R₃, -S(O)₂R₃, -P(O)(R₄)₂ and -C(O)R₅;

each R₃ is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₆-C₁₂ aryl, C₁-C₅ alkoxy, C₆-C₁₂ aryloxy, C₁-C₅ alkylthio, and C₆-C₁₂ arylthio;

each R₄ is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₆-C₁₂ aryl, C₁-C₅ alkoxy, C₆-C₁₂ aryloxy, C₁-C₅ alkylthio, C₆-C₁₂ arylthio, halo and N(R)₂;

each R₅ is independently selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₆-C₁₂ aryl, C₁-C₅ alkoxy, C₆-C₁₂ aryloxy, C₁-C₅ alkylthio, C₆-C₁₂ arylthio, OH, SH and N(R)₂;

 R_6 is selected from the group consisting of C_1 - C_5 alkyl, C_6 - C_{12} aryl, C_1 - C_5 alkylthio, C_6 - C_{12} arylthio, -S(O)R₃, -S(O)₂R₃ and -C(O)R₅,

R" is the same as R above:

Q is selected from halogen and -OS(O)₂Q₁; wherein Q₁ is selected from C₁-C₄ alkyl, C₁-C₄ perfluoroalkyl, phenyl, p-methylphenyl; and

m is, 2, 3, 4, or 5.

19. The process of any one of claims 11 to 18, wherein

X is absent;

B is C2-C5 acyl;

X' is NR;

n is 1;

B' is phenylene; and

10 R is H;

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wherein the substituents directly attached to the phenylene ring may be in a para-, meta- or ortho- relationship.

20. The process of claim 19, wherein said compound is:

$$CO_2$$
 R_10
 R_7
 R_7
 R_8
 R_9
 R_8
 R_9
 $R_$

wherein R_7 to R_{10} are independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_6 - C_{12} aryl, halogen, hydroxy, amino, nitro, carboxy, C_1 - C_5 alkoxy, $-OS(O)_2R_3$ and $-NHC(O)CH_2Q$ wherein Q is halogen, $-OS(O)_2CH_3$, $-OS(O)_2C_6H_5$ and $-OS(O)_2$ -p tolyl; and wherein, when any one of R_7 to R_{10} is C_1 - C_5 alkyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, $-OS(O)_2R_3$ it is capable of forming a fused ring with the phenylene; and further wherein, at least one of R_7 to R_{10} is C_1 - C_5 alkyl, C_6 - C_{12} aryl, C_1 - C_5 alkoxy, or $-OS(O)_2R_3$, in combination with at least any one other of R_7 to R_{10} , is capable of forming a fused ring with the phenylene.

- 21. The process of claim 20, wherein R_7 to R_{10} are independently selected from the group consisting of hydrogen, halogen, hydroxy, amino, nitro, cyano, carboxy, C_1 - C_5 alkoxy, methyl, ethyl, isopropyl, tert-butyl, phenyl and -NHC(O)CH₂Q wherein Q is halogen, -OS(O)₂CH₃, -OS(O)₂C₆H₅ and -OS(O)₂-p tolyl.
- 22. The process of claim 19 or 20, wherein the arsenoxide (-As=O) group is at the 4-position of the phenylene ring.

23. The process of any one of claims 1 to 22 wherein the compound is selected from the group consisting of:

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$$H_2N$$
 H_2N
 H_3
 H_4
 H_2N
 H_3
 H_4
 H_4
 H_5
 H_5
 H_6
 H_6
 H_7
 H_8
 H

24. The process of any one of claims 1 to 19 wherein the compound is represented by 5 Formula VII:

$$H_3N$$
 CO_2
 H_3N
 CO_2
 H_3N
 CO_2
 H_3N
 H_3N

wherein .G is selected from the group consisting of: hydrogen, halogen, hydroxy, amino, nitro, carboxy, C_1 - C_5 alkoxy, C_1 - C_5 alkyl and C_6 - C_{12} aryl and -NHC(O)CH₂Q wherein Q is halogen, -OS(O)₂CH₃, -OS(O)₂C₆H₅ or -OS(O)₂-p tolyl.

- 25. The process of claim 24, wherein G is selected from the group consisting of: hydrogen, halogen, hydroxy, amino, nitro, carboxy, C₁-C₅ alkoxy, methyl, ethyl, iso-propyl, tert-butyl, phenyl, and -NHC(O)CH₂Q wherein Q is halogen, -OS(O)₂CH₃, -OS(O)₂C₆H₅ or -OS(O)₂-p tolyl.
- 26. The process of claim 24 or 25, wherein G is selected from the group consisting of hydroxy, fluorine, amino, and nitro.
- 27. The process of any one of claims 1 to 26, wherein the arsenoxide group (-As=O) is replaced by an arsenoxide equivalent as defined herein.
- 28. The process of claim 27, wherein the arsenoxide equivalent is any dithiol reactive species that shows essentially the same affinity towards dithiols as -As=O.